REMARKS

Claims 1 and 23-28 have been allowed. Claims 39-44 have been rejected. Claim 39 has been amended to incorporate a limitation from Claim 1. Accordingly, the Applicants do not believe that any new matter has been added.

Rejection—35 U.S.C. §102

Claims 39-44 were rejected under 35 U.S.C. 102(e) as being anticipated by Margolin et al., U.S. Patent No. 6,359,118. Claim 39 and Claims 40-44 which depend or refer back to Claim 39 are not anticipated by Margolin et al. which does not disclose a crosslinker which is produced by combining a second and first compound in a molar ratio ranging from 10 : 1 to 1 : >1 as now required by Claim 39. Moreover, as explained below, the Margolin molecules are not crosslinkers, but merely cross-linkable molecules.

The rejection assumes that the claimed crosslinker is already described in Margolin, as a combination of glutaraldehyde and a diamino-alkane is described in the passage of column 25, line 67-column 26, line 3. However, Margolin further exemplifies this diamino-octane pre-treated glutaraldehyde on column 27, lines 3-66, in particular lines 27-29, wherein it is indicated that the pre-treatment was performed using the same molar ratio of glutaraldehyde and diamino-octane. It is to be understood that by combining equimolar amounts of glutaraldehyde and diamino-octane, a linear polymer can be obtained, in line with the teaching of the present invention, however, as such a polymer would consist of the same number of glutaraldehyde and diamino-octane units, it would intrinsically have a single terminal aldehyde-group and, the other end of the polymer, a free primary aminogroup from the terminal diamino-octane moiety.

On the other hand, a crosslinker according to the present invention would be prepared by using glutaraldehyde and diamino-octane using an excess of glutaraldehyde, resulting in a

linear polymer, having, at both ends, a functional aldehyde group, as explained in paragraph 32 of the application as published, as well as in figure 2 of the published application. See line 29 of paragraph 32:

> *In order to avoid free primary amino groups, the ratio should preferably not equal 1 or being lower than 1. Free amino groups cannot participate in the envisaged protein crosslinking in the preparation of CLEAs.*

Indeed, except for glutaraldehyde, none of the molecules that can optionally be obtained according to the teaching of Margolin, would have more than a single functional aldehyde group. A molecule with a single functional group would not be capable of crosslinking proteins to one another. However, and this is what Margolin intends to do, molecules are provided that can as such be linked to a protein, in particular crosslinked glycoprotein crystals, in order to confer improved dissolution characteristics. Once linked to the protein, the molecules according to Margolin's teaching cannot be further crosslinked since the single functional group has been used up by linking to the protein. Therefore, by the use of such molecules proteins cannot be crosslinked to one another.

The Applicants respectfully traverse the argument that the prior art linking agent, being a combination of glutaraldehyde and diamino-octane, can be used to crosslink a protein molecule to another protein molecule. The rejection cites column 5, lines 55-37, wherein the first crosslinking of Margolin is discussed, i.e., crosslinking glycoprotein crystals by a carbohydrate. The carbohydrate has indeed two functional crosslinkable aldehyde groups (glutaraldehyde). However, the combination of glutaraldehyde and diamino-octane is only described for the second linking procedure, which, as discussed above, does not lead to crosslinking of proteins to one another, but only to linking of the said combined molecule to a single protein, see column 25, line 61-column 26, line 3 of Margolin. Thus, the molecules as proposed by Margolin are not crosslinkers, but are simply linkable molecules.

If Claim 39 is allowable, then so should the remaining claims which depend from or refer back to Claim 39. Moreover, since the molecules as described by Margolin are not capable of crosslinking two protein molecules to one another, then Claim 42 should be allowable on this basis. Accordingly, the Applicants respectfully request that this rejection now be withdrawn.

Information Disclosure Statement

The Applicants respectfully request that the Examiner initial the IDS submitted February 28, 2002. While the IDS form was signed, the citation for EP 1 088 887 was not initialed.

CONCLUSION

In view of the above amendments and remarks, the Applicants respectfully submit that this application is now in condition for allowance. Early notification to that effect is earnestly solicited.

Respectfully submitted,

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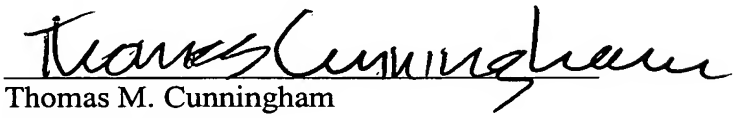
Norman F. Oblon



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